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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/808,496	03/24/2004	Anuschirvan Peyman	446.016-DIV	5709

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HEDMAN & COSTIGAN P.C.
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	PAPER NUMBER
1624	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/808,496	PEYMAN ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8-29-06 (RCE)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-6 and 8* is/are allowed.

6)☒ Claim(s) *11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8-29-06 has been entered.

Applicant's preliminary amendment has been fully considered. As stated in the previous actions, claim 11 was inadvertently included, but should have been withdrawn. However, since no art found for compound claims, claim 11 will be examined.

Claims 7, 9 and 10 have been cancelled.

Claims 1-6, 8 and 11 are pending.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement: Claim 11 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating osteoporosis using the claimed compounds does not reasonably provide enablement for a method of treating any bone

disorder using said compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The Breadth of the claims: Claim 11 recites: "A method of treating bone disorders in warm-blooded animals comprising administering to warm-blooded animals in need thereof an amount of the compound of claim 1 sufficient to treat bone disorders." The term **"bone disorders"** encompasses osteoporosis as well as arthritis and many others, see the following excerpt:

> **[0237]** Bone diseases for whose treatment and prevention the compounds of the formula I according to the invention can be employed are especially osteoporosis, hypercalcemia, osteopenia, for example caused by metastases, dental disorders, hyperparathyroidism, periarticular erosions in rheumatoid arthritis and Paget's disease. In addition, the compounds of the formula I can be used for the allevation, avoidance or therapy of bone disorders which are caused by a glucocorticoid, steroid or corticosteroid therapy or by a lack of sex hormone(s). All these disorders are characterized by bone loss which is based on the inequilibrium between bone formation and bone destruction and which can be favorably influenced by the inhibition of bone resorption by osteoclasts. The compounds of the formula I and/or their

Furthermore, formulae IIIa, IIIb and IIIc of claim 1 cover a myriad of compounds. Thus, the scope of claim 11 is not only broad in term of various bone disorders but also broad in term of a large number of compounds to select from.. Therefore, the scope of claim 11 is unduly broad.

The amount of direction or guidance presented: The specification describes a bioassay for the inhibition of vitronectin (Vn). Six compounds were tested for such an inhibition; however, they were all purine compounds. Although all tested compounds have naphthyridinyl-piperidine substituent just as those claimed herein, the purine portion distinguishes the test compounds from all those claimed herein. That is, the specification provides no adequate support for how to use **representative** scope of naphthyridinyl-piperidine

claimed which can carry a variety of bicyclic rings as in formulae IIIa, IIIb and IIIc. Receptor binding is known to be structure-sensitive in general. Note **In re Surrey** 151 USPQ 724 regarding sufficiency of disclosure for a Markush group where as herein no examples of a diverse nature have been made much less tested to show the requisite activity needed to practice the invention. Also, see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as pharmaceutical art.

The state of the prior art: Currently, the state of the art reveals that vitronectin antagonists can inhibit osteoclast adhesion, and thus, inhibit bone resorption as evident by the article of **Gowen et. al.** The closest vitronectin antagonist is that of Merck, which has the naphthyridinyl-piperidine portion, but lacks the bicyclic portion as in the claimed formulae IIIa, IIIb and IIIc. Furthermore, the side effect profile of vitronectin antagonist has yet to be determined. The teaching of Gowen et. al. also does not relate the inhibition of vitronectin to other bone disorders such as those listed in the specification. Thus the state of the art does not support the broad scope of treatment using a myriad of compounds as claimed herein.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to carry out extensive research to select an effective compound from the large Markush group of the three formulae claimed herein. Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50}, therapeutic index and pharmacokinetic

profile for each compound. Given a large Markush group of the three claimed formulae, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting pathways, or biological factors that are sometimes genetically unique to individuals. In the instant case the claimed formulae IIIa, IIIb and IIIc do not have structural similarity with the tested compounds to warrant activity on vitronectin receptor, thus the skilled chemist would have to carry out undue experimentation to use compounds of the claimed formulae.

Note, the Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the **full scope** of the invention without 'undue experimentation'".

Allowable Subject Matter

Claims 1-6 and 8 are allowed as being drawn to compounds with the combination of naphyridinyl-(piperidinyl or cyclohexanyl)-(fused pyrimidine or pyridine) that are not taught or fairly suggested by the prior art of record.

References on PTO-892

References cited on PTO-892 show state of the art only because they fail to teach the combination of rings as represented by the instant formulae IIIa, IIIb and IIIc.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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12-21-06

Tamthom N. Truong
Examiner
Art Unit 1624

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600